

FIG. 2A

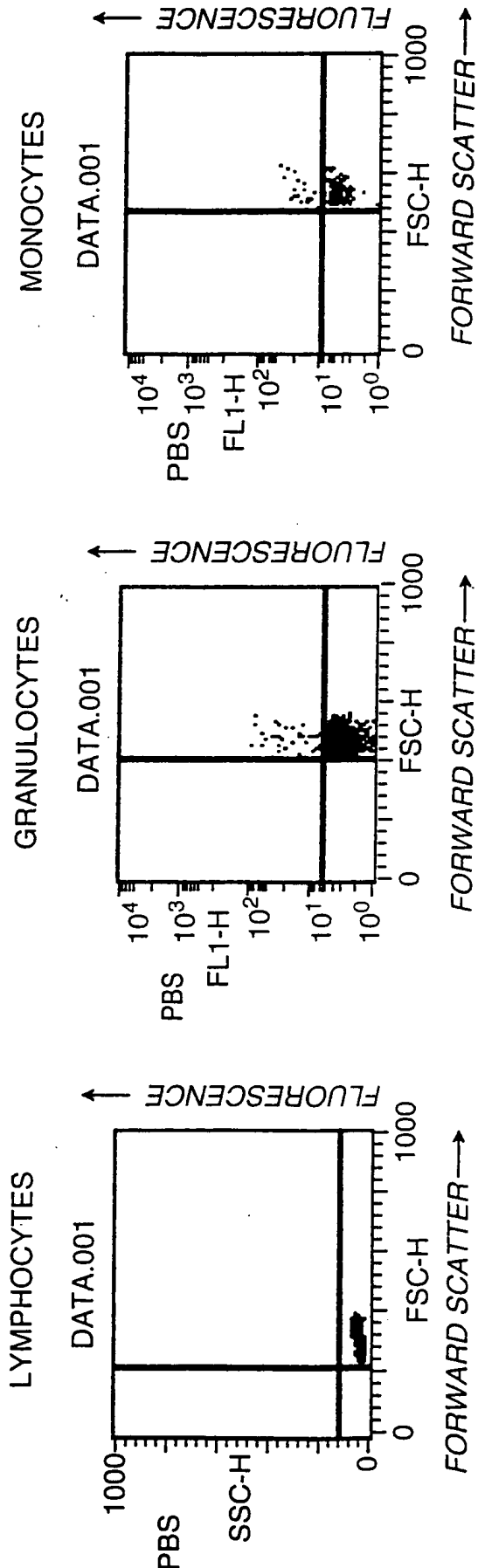


FIG. 2B

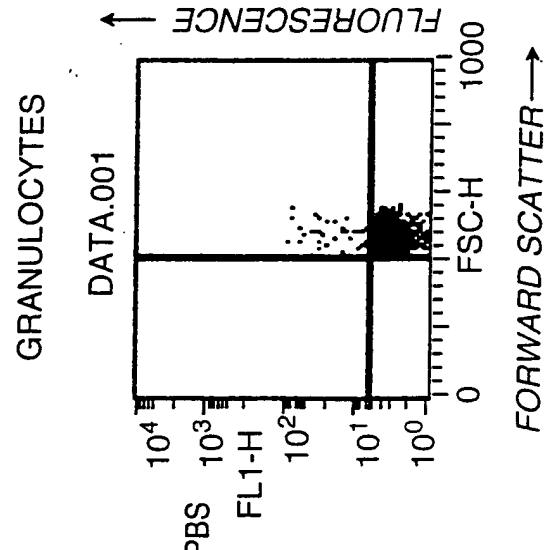


FIG. 2C

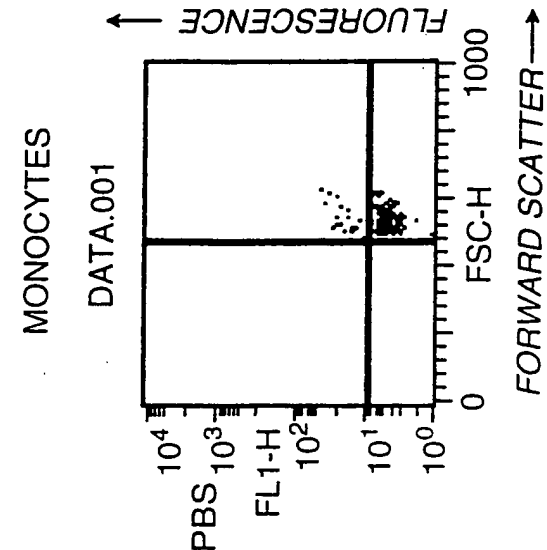


FIG. 2D

LYMPHOCYTES

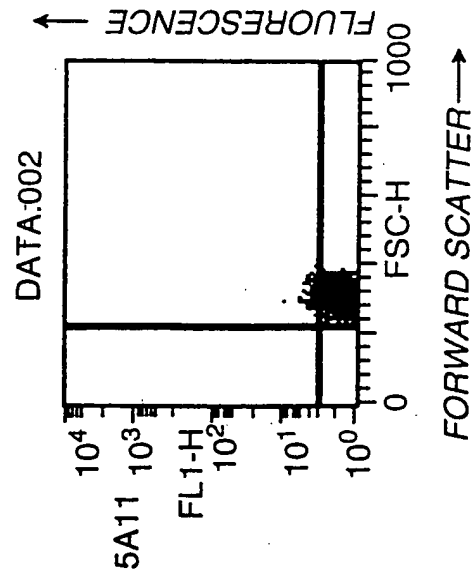


FIG. 2E

GRANULOCYTES

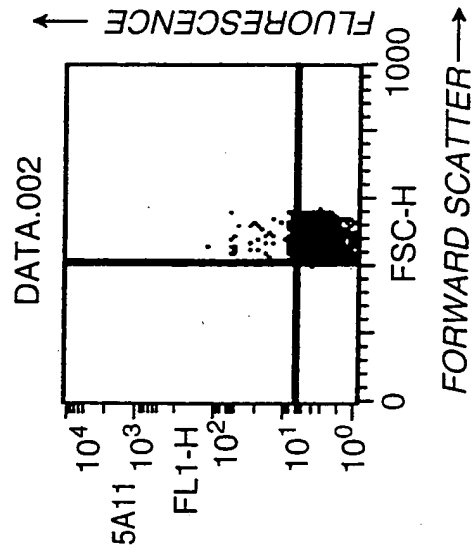


FIG. 2F

MONOCYTES

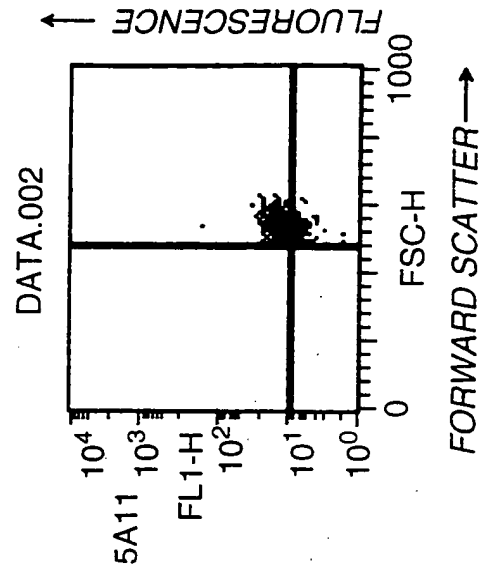


FIG. 2G

LYMPHOCYTES

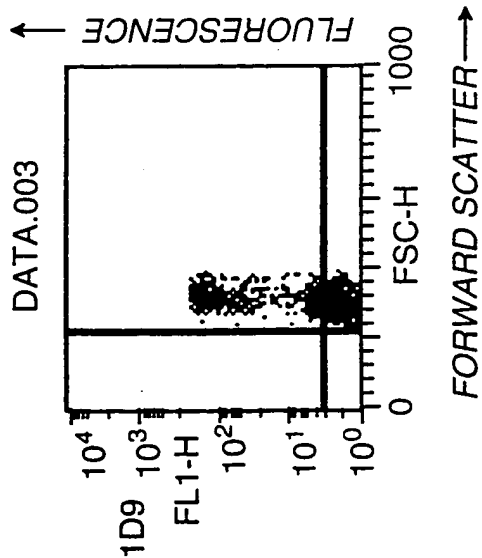


FIG. 2H

GRANULOCYTES

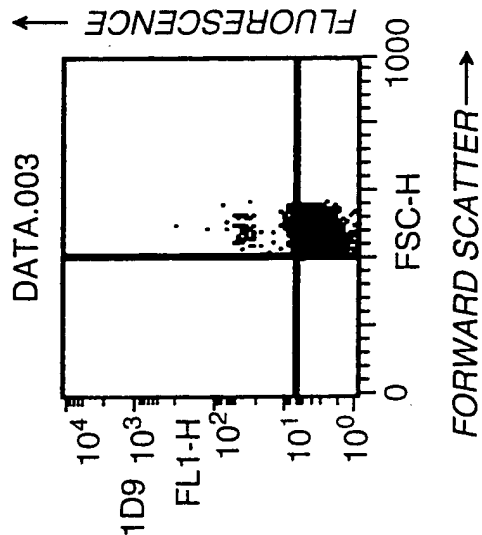


FIG. 2I

MONOCYTES

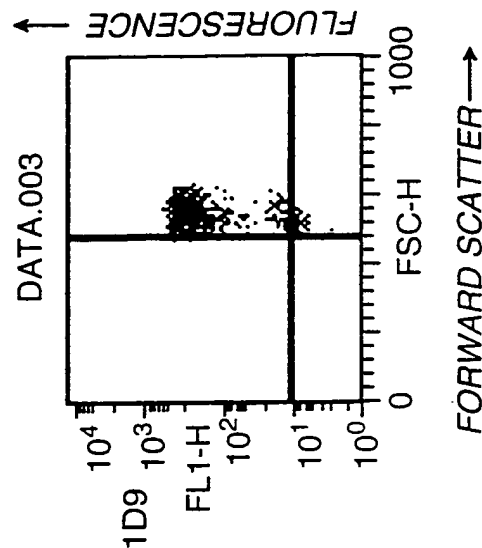




FIG. 2J

LYMPHOCYTES

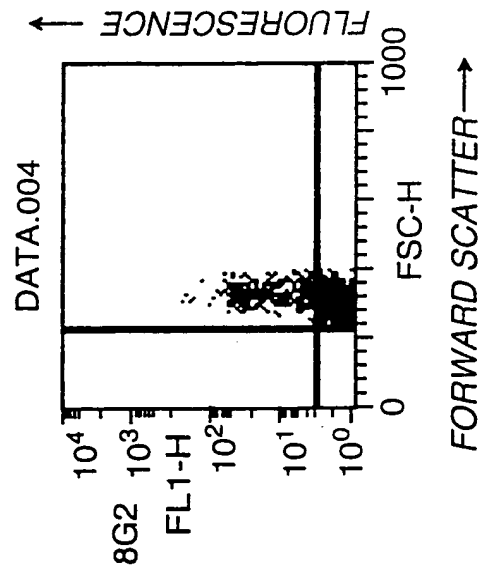


FIG. 2K

GRANULOCYTES

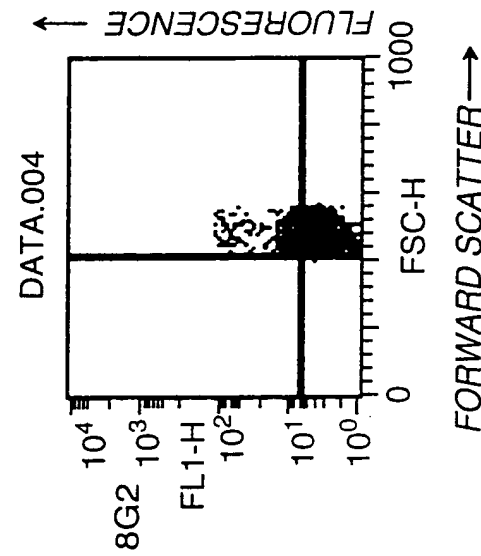


FIG. 2L

MONOCYTES

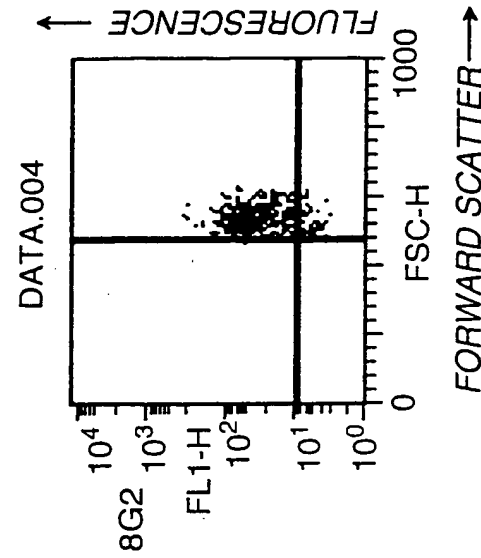


FIG. 3A

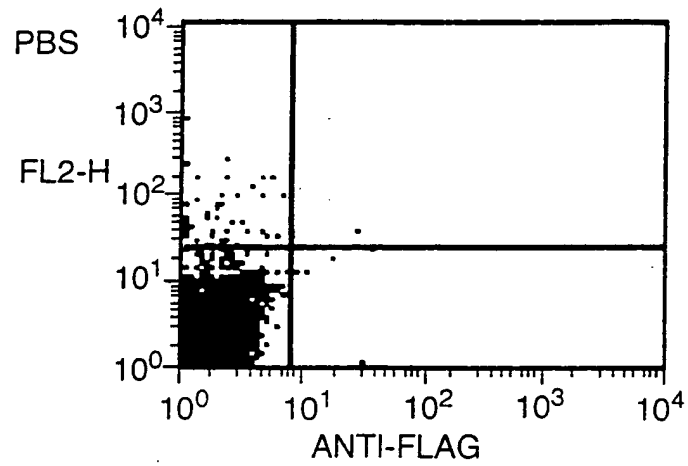


FIG. 3B

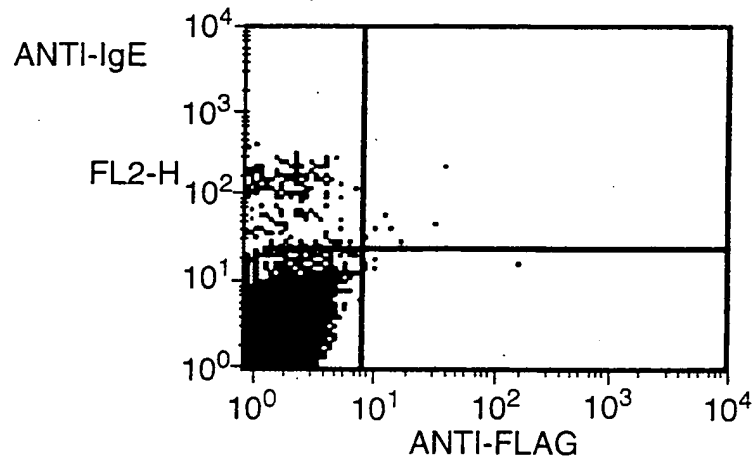


FIG. 3C

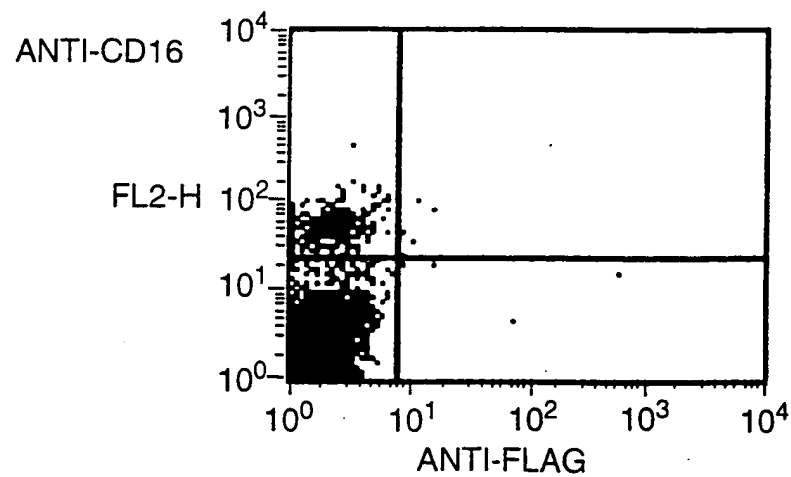


FIG. 3D

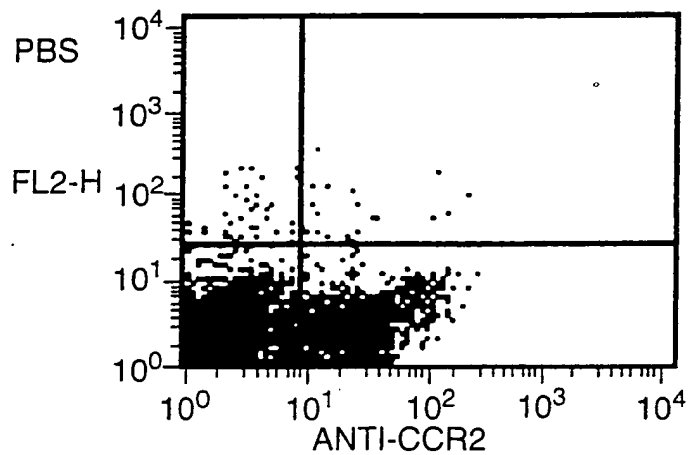


FIG. 3E

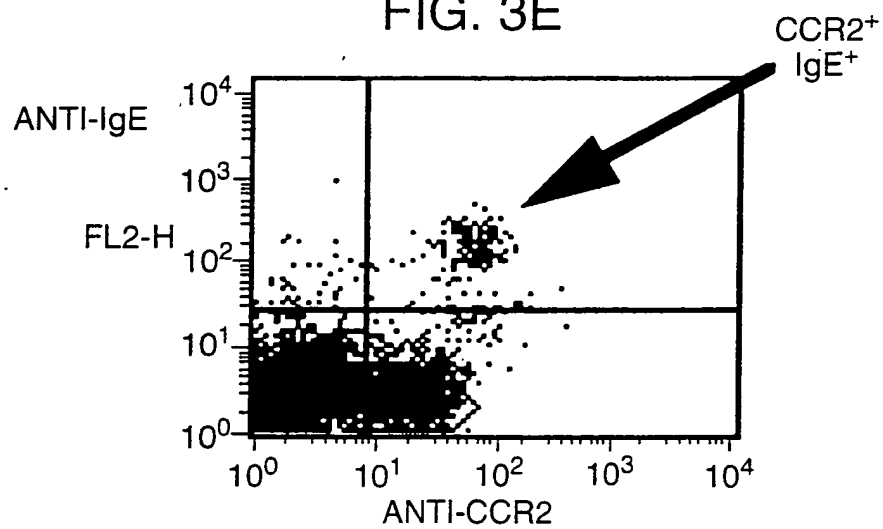


FIG. 3F

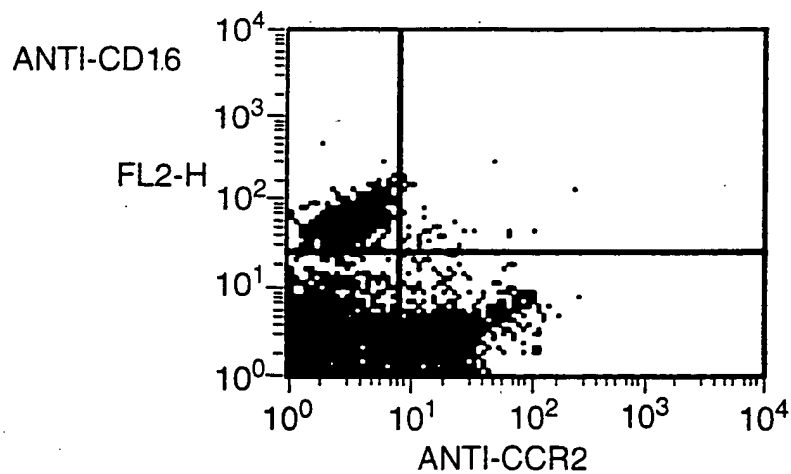


FIG. 3G

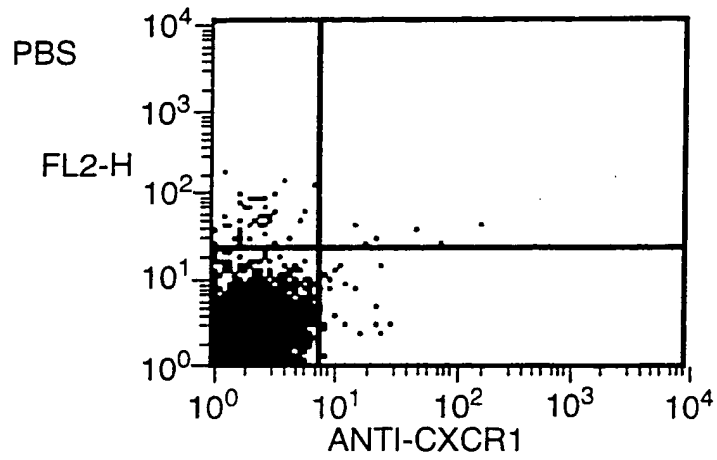


FIG. 3H

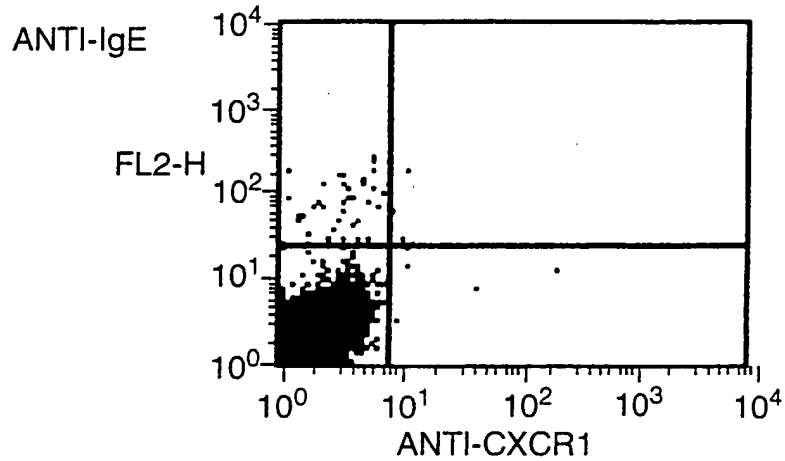
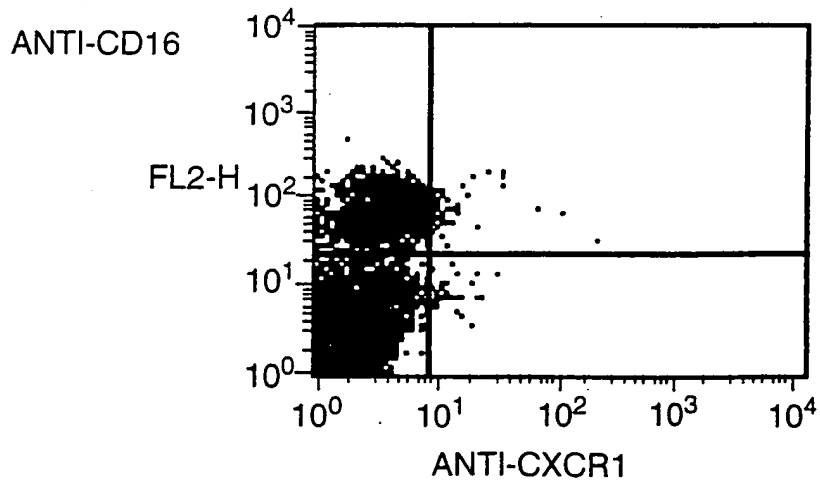


FIG. 3I



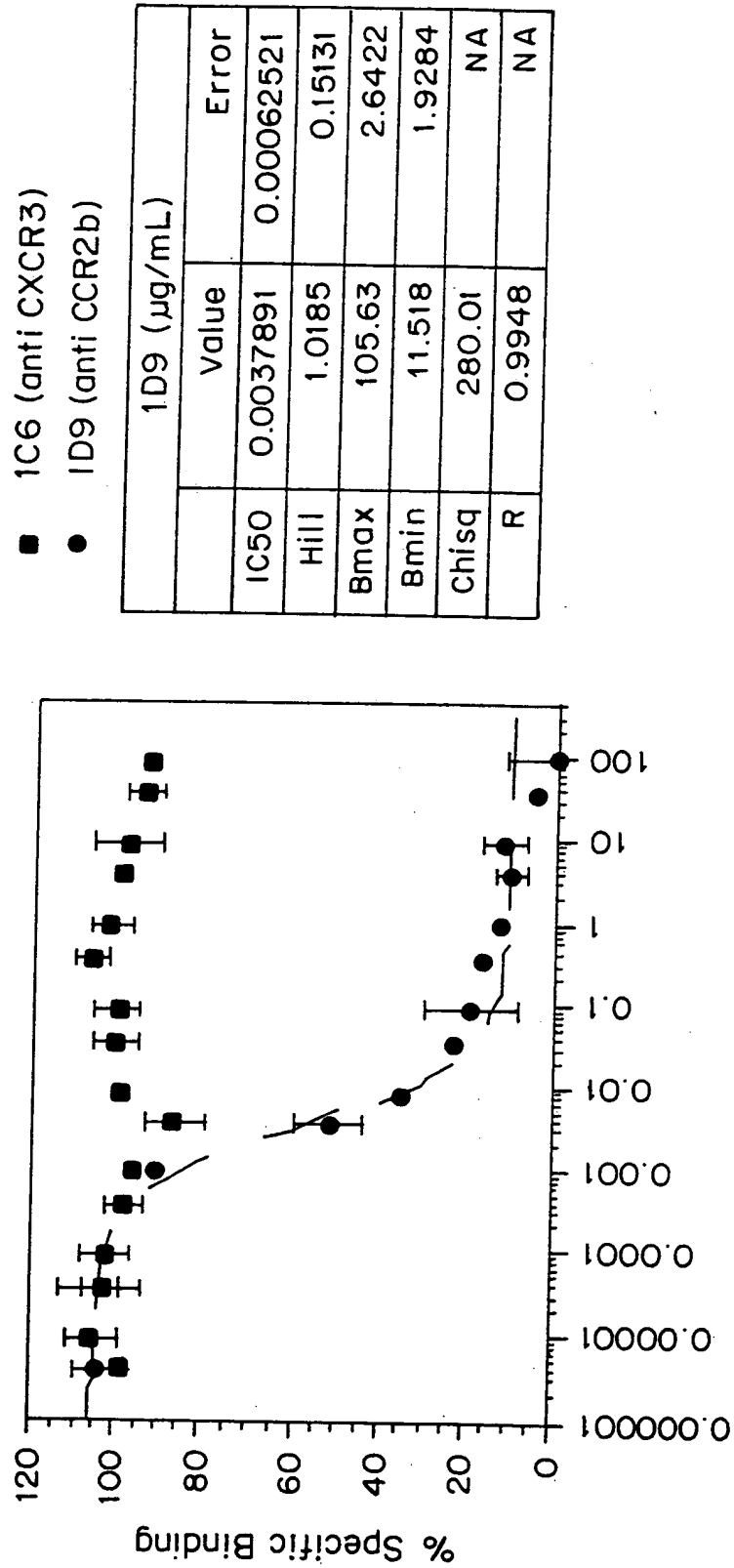


FIG. 4

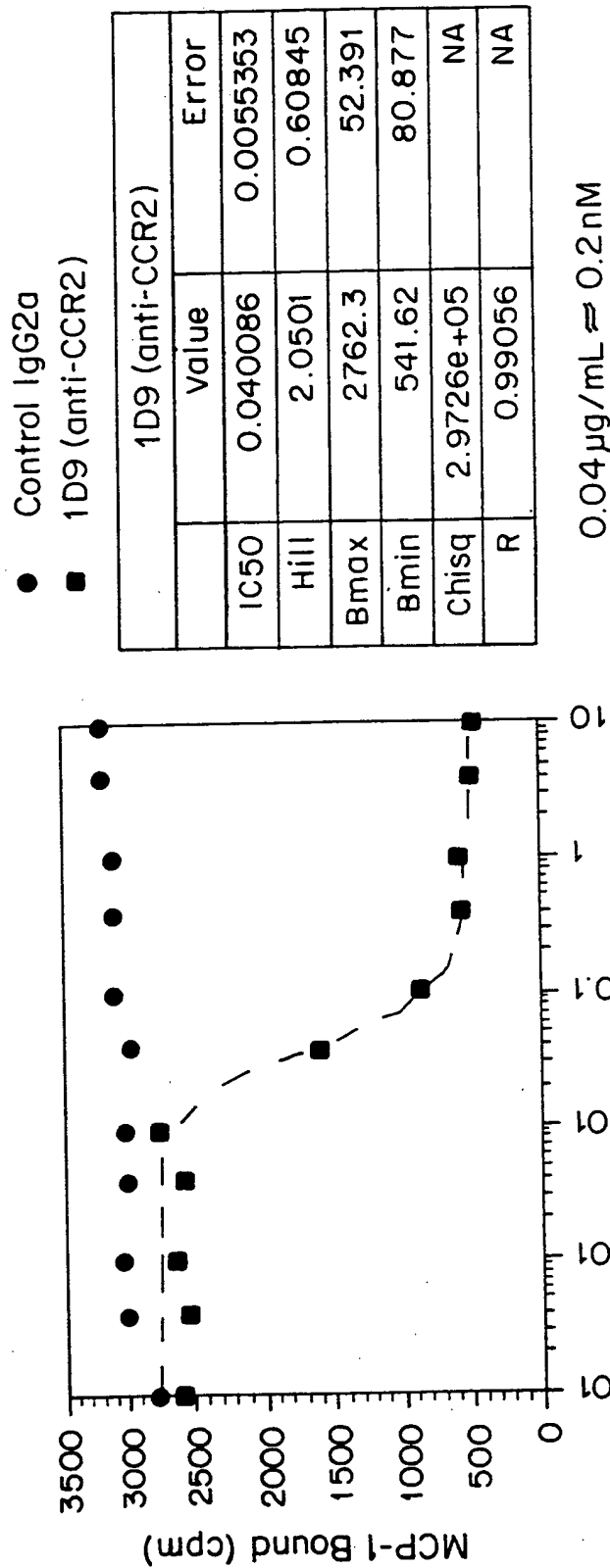


FIG. 5

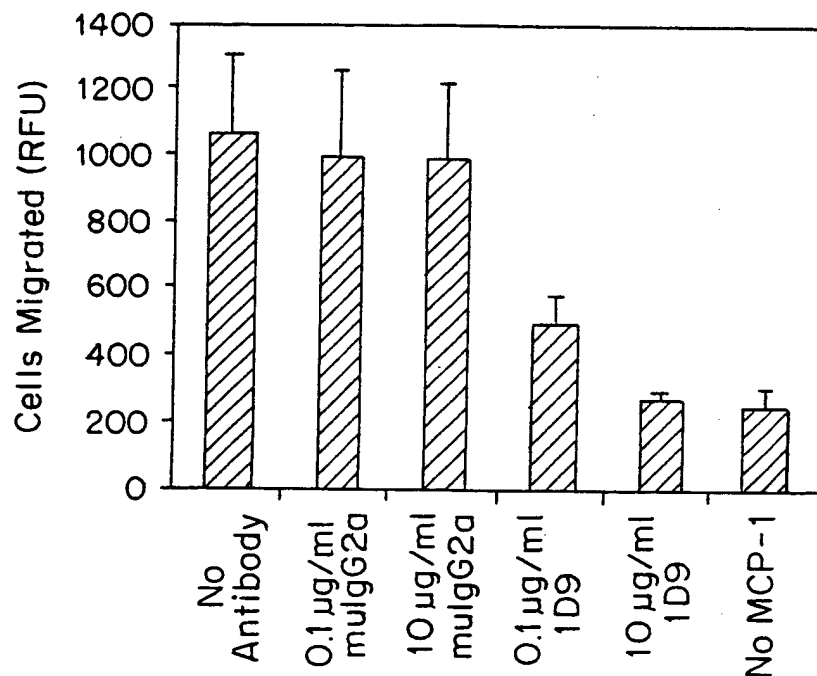


FIG. 6A

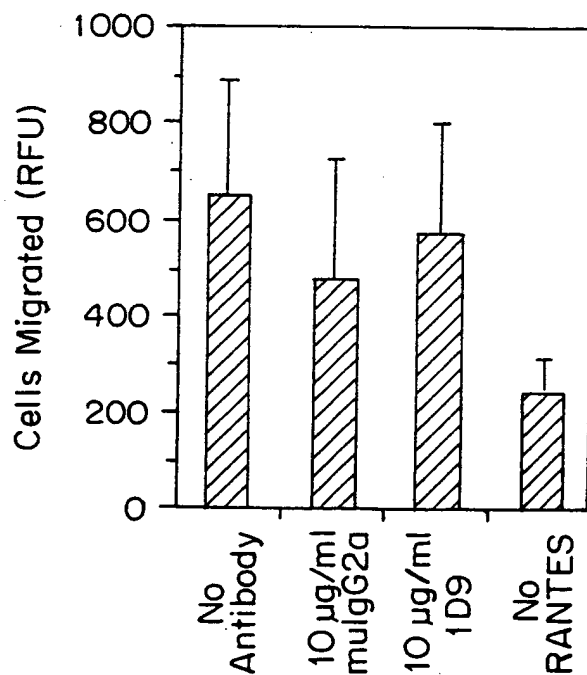


FIG. 6B

Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

```

1   DVVMTQTPLT LSVTVGHPAS ISCKSSQSLL DSDGKTFLNW LLQRPQGSPK

51  RLIYLVSKLD SGVPDRFTGS GSGTDFTLKI SRVEAEDLGV YYCWQGTHFP

101 YTFGGGTKLE IK
    
```

Figure 7



1      EVQLVESGGG LVQPKGSLKL SCAASGFSFN **AYAMNWVRQA** PGKGLEWVAR

51    IRTKNNNYAT **YYADSVKDRY** TISRDDSESM LFLQMNNLKT EDTAMYYCVT

101 **FYGNGVWG**TG TTVTVSS

Figure 8

**Chothia Canonical Classes**

- L1 (16 amino acids) = Class 4  
Key residues: 2(V), 25(SA), 29(L), 33(L), 71(F)
- L2 (7 amino acids) = Class 1  
Key residues: 48(IV), 51(AT), 52(ST), 64(G)
- L3 (9 amino acids) = Class 1  
Key residues: 90(QNH), 95(P)

**Martin Canonical Classes**

- L1 (16 amino acids) = Class 4/16A  
Key residues: 2(V), 4(ML), 23(C), 25(SSP), 26(SN),  
27(Q), 29(LI), 30A(HL), 30B(S),  
30C(NDS), 30D(G), 32(YS), 33(LF),  
34(HEN), 35(W), 51(V), 71(F), 88(C),  
90(Q), 92(TS), 93(H)
- L2 (7 amino acids) = Class 1/7A  
Key residues: 23(C)
- L3 (9 amino acids) = Class 1/9A  
Key residues: 2(IVL), 3(VQLE), 4(ML),  
28(SNDTE), 30(DYLVISNFGHT),  
31(SNTKG), 32(FYNAHSR),  
33(MLVIF), 88(C), 89(QSGFL),  
90(QNH), 91(NFGSRDHTYV),  
92(NYWTSRQHAD),  
93(ENGHTSRAQHAD),  
94(DYTVLHNNIWPS), 95(P),  
96(PLYRIWF), 97(T), 98(F)

Figure 9

### Chothia Canonical Classes

- H1 (5 amino acids) = Class 1  
Key residues: 24(AVG), 26(G), 27(FY)
- H2 (19 amino acids) = Class 4  
Key residues: 54(S), 55(Y), 71(R)

### Martin Canonical Classes

- H1 (5 amino acids) = Class 1/10A  
Key residues: 2(VIG), 4(LG), 20(LIMV), 22(C),  
24(TAGVS), 26(G), 29(IFLS),  
32(IHYFTNCED), 33(AWGTLV),  
34(TVMW), 35(HENQSYT), 36(W),  
48(IMLV), 51(LIVTSN),  
69(ILFMV), 78(ALVYF), 80(LM),  
90(YF), 92(C), 94(RKGSNH),  
102(YHVISDG).
- H2 (19 amino acids) = Class ?/12B  
Key residues: 47(W), 50(RQ), 51(I), 59(Y), 69(I),  
71(R), 78(LV)

Figure 10

[illegible]

## Key

1D9 V <sub>K</sub>	Mouse 1D9 V <sub>K</sub> region
HF-21/28 V <sub>K</sub>	Chosen human framework acceptor V <sub>K</sub> region sequence with mismatches to the 1D9 V <sub>K</sub> region highlighted.
1D9RK <sub>A</sub> V <sub>K</sub>	CDR grafted 1D9 V <sub>K</sub> region, with no back mutations but with the added human lysine residue at position 107 (i.e. 107K).
1D9RK <sub>B</sub> V <sub>K</sub>	CDR grafted 1D9 V <sub>K</sub> region, with back mutations at F36L and Q37L, and the additional 107K insertion.
1D9RK <sub>C</sub> V <sub>K</sub>	CDR grafted 1D9 V <sub>K</sub> region, with back mutations at F36L, Q37L and Q100G, and the additional 107K insertion.
1D9RK <sub>D</sub> V <sub>K</sub>	CDR grafted 1D9 V <sub>K</sub> region, with back mutations at F36L, Q37L, Q100G and Q17H, and the additional 107K insertion.
1D9RK <sub>E</sub> V <sub>K</sub>	CDR grafted 1D9 V <sub>K</sub> region, with back mutations at F36L, Q37L and Q17H, and the additional 107K insertion.

### Figure 11

## Key

1D9 V <sub>H</sub>	Mouse 1D9 V <sub>H</sub> region.	Chosen human framework acceptor V <sub>H</sub> region sequence with mismatches to the 1D9 V <sub>H</sub> region highlighted.
4B4'CL V <sub>H</sub>		
1D9RH <sub>A</sub> V <sub>H</sub>	CDR grafted 1D9 V <sub>H</sub> region, with no back mutations.	
1D9RH <sub>B</sub> V <sub>H</sub>	CDR grafted 1D9 V <sub>H</sub> region, with back mutations at T28S and N30S.	
1D9RH <sub>C</sub> V <sub>H</sub>	CDR grafted 1D9 V <sub>H</sub> region, with back mutations at T28S, N30S, G49A and F67Y.	
1D9RH <sub>D</sub> V <sub>H</sub>	CDR grafted 1D9 V <sub>H</sub> region, with back mutations at T28S, N30S, G49A, F67Y and T93V.	

### Figure 12

**Figure 13**

**Figure 13**

Applicants: Theresa O'Keefe et al.

## HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF USE THEREFOR

Sequence Name	Identical Residues	Amino Acid Sequence
1D9 V <sub>H</sub>	117	EVQLVESGGGLVQPKGSLKLSCAASGFSFNAYAMN--WVRQAPGKLEWVARIRTKNNYATYYADSVKDRYTISRDSSESLFLQMNNLKTEDTAMYYCVTF
MRL-RF24BG	86	.....VWWRM.....T.T.....S.SS.....S.SS.....Q...Y.....F.....Q...Y.....I-
V(H)22.1	70	..K.E.....G.M...V...T.SN.W.S.....S.E.....Q.L.SD...H.E..G.F.....K.SVY.....RA..GI...TG-
V11/pBV19B4	66	..K.....G...R...T...T.TD.Y.S.....P...A...LGF...N.A.G.T.E.SA...G.F.....N.Q.I.Y...T.RA..S.T...AR-
VH7183(Vh69.1)	66	..K.....K.G.....T.SS.T.S.....S.E.R.....T.SS--GGSY...P...G.F.....NAKNT.Y...SS..S...TR-
VH10-19	65	D.K.....K.G.....T.SS.T.S.....T.E.R.....T.SS--GGSY...P...G.F.....NAKNT.Y...SS..S...TR-
VHE4-psi	65	L.....G.R.....T.SS..S.....T.E.R.....A.S.--DGSFI.XP.T.G.F.....NAKNT...SS.RY...LR-
V(H)50.1	65	..K.....G.....T.SD.Y.Y.....T.E.R.....Y.SN--GGGS...P.T.G.F.....NAKNT.Y...SR..S...AR-
V3	65	..K.....GA..R...S...T.TD.Y...HRP...P...L.L.N.A.G.I.E.SA.M.G.F...N.Q.I.Y...T.S..S.T...ARD
V1/pBV132	64	..K.....G...R...T...T.SDFY.E.....P...R...I.AS.N.A.D.T.E.SA...G.FIV...T.Q.I.Y...A.RA...I...AR-
VH283	64	M.....K.G.....T.SS.T.S.....T.E.R.....T.SS--GGGN...P...G.F.....NAKNT.Y...SS.RS...L...AR-
V(H)37.1	63	..K.....K.G.....T...T.SS.G.S.....T.E.R.....T.SG--GGSY...P...G.F.....NAKNT.Y...SS.RS...L...AR-
V13	61	..K.M.....GA..R...E...T.TD.Y.S.....L.R.SP.L.L.N.A.G.T.E.SA...G.F...N.QNI.Y...T.RA.AS.T...AKD
V-H 441/V441	59	..K.L.....G.....D.SR.W.S.....T.D.R...L..T.NS--GGGS...P...G.F.....NAKNT.Y...SKVRS...L...AR-
68-5N	59	-----K.G.....T.SS.G.S.....T.E.R.....T.SS--GGSY...P...G.F.....NAKNT.Y...SS..S...AR-
76-1BG/VH7183.9	58	-----K.G.....T.SSFG.H.....E.....Y.SS--GSSTI...T.G.F...NPKNT...TS.RS...AR-
61-1P	58	-----K.G.....T.SS..S.....T.E.R.....S.S--GGGS...P...G.F...NARNI.Y...SS.RS...AR-
57-1M/VH7183.12	58	-----K.L.....G..N.....D.SR.W.S.....A.....Q..IGE.NP--GSSTIN.TP.L.KFI...NAKNT.Y...SKVRS...L...AR-
V(H)55	56	-----K.G.....T.SS.T.S.....T.E.R.....Y.SN--GGGS...P.T.G.F...NAKNT.Y...SS..S...AR-
VH7183.13	55	-----K.G.....T.SS.T.S.....T.E.R.....Y.SN--GGGS...P.T.G.F...NAKNT.Y...SS..S...AR-

Figure 14

### Amino Acid Sequence

[illegible]

### Figure 15



Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Name	ID	Surface	Core	Kabat CDR	FR	FR Surface	Core FR	FR Near CDR	Vernier	V <sub>K</sub>	J Chain	Closest Human Germline Gene	L1 Len	L2 Len	L3 Len	L1 Class	L2 Class	L3 Class
1D9 V <sub>K</sub>	100.0	30	82	32	82	22	60	33	14	100	14		16	7	9	4	1	1
036521	90.4	27	76	28	75	19	56	31	13	90	13	DPK19-A1+	Same	Same	Same	Same	Same	Same
II.66	78.8	25	67	22	69	18	52	30	13	80	12	DPK18-A17+	Same	Same	Same	Same	Same	?
RPMI6410	78.8	25	67	22	69	18	52	30	13	79	12	DPK18-A17+	Same	Same	Same	Same	Same	?
ZM1-1	78.8	25	66	21	68	18	52	30	13	79	12	DPK18-A17+	Same	Same	Same	Same	Same	Same
VL clone	78.1	25	66	21	68	18	52	30	13	79	12	DPK18-A17+	Same	Same	Same	?	Same	Same
54																		
HF-21/28	79.3	24	66	21	68	18	52	30	13	78	12	DPK18-A17+	Same	Same	Same	Same	Same	Same
SpA2-08	77.9	24	65	21	68	18	51	30	13	77	12	DPK18-A17+	Same	Same	Same	?	Same	Same
II.30	77.9	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same	Same	Same	Same	Same	Same
HUNVK	77.9	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same	Same	Same	Same	Same	Same
O-81	75.7	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same	Same	Same	Same	Same	?
ToP309	74.8	24	64	20	68	18	51	29	12	76	12	DPK12-A2+	Same	Same	Same	?	Same	?
ToP218	74.8	24	64	20	68	18	51	29	12	76	12	DPK12-A2+	Same	Same	Same	?	Same	?
SpA3-02	76.1	24	63	20	68	18	51	29	12	76	12	DPK18-A17+	Same	Same	Same	?	Same	?
II.37	75.2	24	63	20	68	18	51	29	12	76	12	DPK18-A17+	Same	Same	Same	?	Same	Same
CUM	73.9	24	63	20	68	18	50	29	12	75	12	DPK36-Chr22 4	Same	Same	Same	Same	Same	Same
VL clone	74.6	24	62	20	67	18	50	29	12	75	12	DPK18-A17+	Same	Same	Same	3	Same	Same
51																		
II.20	75.2	23	62	20	67	18	50	29	12	75	12	DPK18-A17+	Same	Same	Same	?	Same	Same

Figure 16

## Amino Acid Sequence

[illegible]

**Figure 17A**

**Figure 17B**

Name	ID	All	Surface	Core	Kabat CDR	FR	Surface	Core	FR	Near CDR	V <sub>H</sub>	J Chain	Closest Human Germline Gene	H1 Size	H2 Size	H3 Size	H1 Class	H2 Class
1D9 V <sub>H</sub>	100.0	117	29	84	30	87	21	65	30	16	100	17		5	19	6	1	4
030094	67.7	86	19	67	15	72	17	57	26	12	75	13	DP-29-122+	Same	Same	16	Same	Same
N51P8	68.3	86	18	66	15	72	16	57	25	12	75	13	DP-29-122+	Same	Same	15	?	Same
IW2-91	67.5	85	18	65	15	72	16	56	25	12	75	12	DP-29-122+	Same	Same	15	Same	Same
H2-46	66.7	84	18	65	15	72	16	56	25	12	75	12	DP-29-122+	Same	Same	15	Same	Same
039158	72.2	83	17	64	15	71	15	56	25	12	74	12	DP-29-122+	Same	Same	15	Same	Same
038064	65.6	82	17	64	14	71	15	56	25	11	74	12	VH26Rabbits+					
038062	64.6	82	17	63	14	71	15	56	25	11	73	12	VH26Rabbits+					
32.B9	64.6	82	17	63	14	71	15	56	25	11	72	12	VH26Rabbits+	Same	17	19	Same	3
038062	64.6	82	17	63	14	71	15	56	25	11	72	12	VH26Rabbits+					
034514	69.8	81	17	63	14	70	15	56	25	11	72	12	VH26Rabbits+					
038066	65.3	81	16	63	14	70	15	55	25	11	71	12	VH26Rabbits+					
035365	65.9	81	16	63	14	70	15	55	25	11	71	12	VH26Rabbits+					

**Figure 18A**

Applicants: Ther sa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Name	ID	All	Surface	Core	Kabat CDR	FR	FR Surface	Core FR	FR Near CDR	Vernier	V <sub>H</sub>	J Chain	Closest Human Germline Gene	H1 Size	H2 Size	H3 Size	H1 Class	H2 Class
Hb-5	69.2	81	16	63	14	69	15	55	25	11	71	12	VH26Rabbits+	Same	17	16	Same	3
4G12	64.8	81	16	63	14	69	15	55	25	11	71	12	VH26Rabbits+	Same	17	16	Same	3
VH clone 39	66.7	80	16	63	14	69	14	55	25	11	71	12	VH26Rabbits+	Same	17	11	Same	3
040094	62.5	80	16	63	14	69	14	55	25	11	71	12	LSG3.1	Same	17	18	Same	3
VH clone 18	63.0	80	16	63	13	69	14	55	25	11	71	12	VH26Rabbits+	Same	17	18	Same	3
UB1-24	67.2	80	16	63	13	69	14	55	25	11	71	12	DP-31-V39P+	Same	17	10	Same	3
029764	64.5	80	16	63	13	69	14	55	25	11	71	12	VH26Rabbits+	Same	17	15	Same	3
IW2-105	64.5	80	16	63	13	69	14	55	25	11	71	12	LSG3.1	Same	Same	13	Same	?
UB1-17	65.0	80	16	63	13	69	14	55	25	11	71	11	LSG3.1	Same	Same	12	Same	?
VH clone 41	66.1	80	16	62	13	69	14	55	25	11	71	11	VH26Rabbits+	Same	17	12	Same	3
4B4'CL	67.2	80	16	62	13	68	14	55	25	11	71	11	LSG3.1	Same	Same	8	Same	?
M26	65.0	80	16	62	13	68	14	55	25	11	71	11	LSG3.1	Same	Same	12	Same	?

Figure 18B

Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Kabat	#	FR or CDR	Mouse 1D9 V <sub>K</sub>	Mouse κ-II	Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK <sub>A</sub>	1D9 RK <sub>B</sub>	Comment
1	1	FR1	D	D*	D		S		D	D	
2	2		V	V	I*		C		V	V	
3	3		V	V	V*		S		V	V	
4	4		M	M	M		C		M	M	
5	5		T	T*	T		C		T	T	
6	6		Q	Q*	Q		C		Q	Q	
7	7		T	T	S	S	S		S	S	
8	8		P	P	P		c		P	P	
9	9		L	L	L		s		L	L	
10	10		T	S	S	S	C		S	S	
11	11		L	L	L*		c		L	L	
12	12		S	P	P	P	c		P	P	
13	13		V	V*	V*		c		V	V	
14	14		T	S	T		c		T	T	
15	15		V	L	P	L	s		L	L	
16	16		G	G	G		c		G	G	
17	17		H	D	E	Q	c		Q	Q	
18	18		P	Q	P		s		P	P	
19	19		A	A	A		c		A	A	
20	20		S	S*	S		c		S	S	
21	21		I	I*	I		c		I	I	
22	22		S	S*	S*		C		S	S	
23	23	FR1	C	C	C		C		C	C	
24	24	CDR1	K	R	R	R	s		K	K	
25	25		S	S*	S*		c		S	S	
26	26		S	S*	S		s		S	S	
27	27		Q	Q	Q		s		Q	Q	
27A	28		S	S	S		s		S	S	
27B	29		L	L	L		c		L	L	
27C	30		L	V	L	V	s		L	L	
27D	31		D	H	H	H	c		D	D	
27E	32		S	S	S		s		S	S	
27F			-	-	x				-	-	
28	33		D	N	D		s		D	D	
29	34		G	G*	G		c		G	G	
30	35		K	N	N	N	c		K	K	
31	36		T	T	N		c		T	T	
32	37		F	Y*	Y	Y	c		F	F	
33	38		L	L*	L		c		L	L	
34	39	CDR1	N	E	N		c		N	N	
35	40	FR2	W	W	W		C		W	W	
36	41		L	Y	Y	F	C		F	L	Δ1

Figure 19A

Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Kabat	#	FR or CDR	Mouse 1D9 V <sub>K</sub>	Mouse κ-II		Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK <sub>A</sub>	1D9 RK <sub>B</sub>	Comment
37	42		L	L		L	Q	c		Q	L	Δ2
38	43		Q	Q*		Q		c		Q	Q	
39	44		R	K		K		c		R	R	
40	45		P	P*		P		s		P	P	
41	46		G	G*		G		s		G	G	
42	47		Q	Q		Q		c		Q	Q	
43	48		S	S*		S		c		S	S	
44	49		P	P*		P		C		P	P	
45	50		K	K		Q	R	c		R	R	
46	51		R	L		L		C		R	R	
47	52		L	L*		L		C		L	L	
48	53		I	I*		I		C		I	I	
49	54	FR2	Y	Y		Y		C		Y	Y	
50	55	CDR2	L	K		L		c		L	L	
51	56		V	V		V	K	c		V	V	
52	57		S	S		S		c		S	S	
53	58		K	N		N		c		K	K	
54	59		L	R		R	N	c		L	L	
55	60		D	F		A	R	c		D	D	
56	61	CDR2	S	S*		S		s		S	S	
57	62	FR3	G	G		G		S		G	G	
58	63		V	V		V		C		V	V	
59	64		P	P		P		C		P	P	
60	65		D	D*		D		S		D	D	
61	66		R	R		R		C		R	R	
62	67		F	F*		F		C		F	F	
63	68		T	S		S	S	C		S	S	
64	69		G	G*		G		C		G	G	
65	70		S	S*		S		C		S	S	
66	71		G	G*		G		C		G	G	
67	72		S	S*		S		s		S	S	
68	73		G	G*		G		C		G	G	
69	74		T	T*		T		C		T	T	
70	75		D	D*		D		C		D	D	
71	76		F	F*		F		C		F	F	
72	77		T	T*		T		c		T	T	
73	78		L	L		L		c		L	L	
74	79		K	K		K		c		K	K	
75	80		I	I		I		c		I	I	
76	81		S	S		S		c		S	S	
77	82		R	R*		R		s		R	R	
78	83		V	V		V		c		V	V	
79	84		E	E		E		s		E	E	
80	85		A	A*		A		c		A	A	
81	86		E	E*		E		s		E	E	
82	87		D	D*		D		c		D	D	
83	88		L	L		V	V	c		V	V	
84	89		G	G*		G		c		G	G	
85	90		V	V		V		c		V	V	
86	91		Y	Y*		Y		c		Y	Y	
87	92		Y	Y		Y		C		Y	Y	
88	93	FR3	C	C		C		C		C	C	

Figure 19B

Kabat	#	FR or CDR	Mouse 1D9 V <sub>K</sub>	Mouse $\kappa$ -II		Human $\kappa$ -II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK <sub>A</sub>	1D9 RK <sub>B</sub>	Comment
89	94	CDR3	W	F		M		c		W	W	
90	95		Q	Q*		Q	M	c		Q	Q	
91	96		G	G		A		c		G	G	
92	97		T	T		L		c		T	T	
93	98		H	H		Q		c		H	H	
94	99		F	V		x		s		F	F	
95	100		P	P*		P	W	c		P	P	
95A			-	P		R				-	-	
95B			-	-		-				-	-	
95C			-	-		-				-	-	
95D			-	-		-				-	-	
95E			-	-		-				-	-	
95F			-	-		-				-	-	
96	101		Y	Y		x	-	c		Y	Y	
97	102	CDR3	T	T*		T	F	c		T	T	
98	103	FR4	F	F*		F		C		F	F	
99	104		G	G		G		c		G	G	
100	105		G	G		Q	Q	c		Q	Q	
101	100		G	G		G		c		G	G	
102	106		T	T		T		c		T	T	
103	107		K	K*		K	R	s		R	R	
104	108		L	L		V		c		L	L	
105	109		E	E		E		s		E	E	
106	110		I	I		I		s		I	I	
106A			-	-		-				-	-	
107	111	FR4	K	K*		K	-	s		K	K	

Figure 19C



Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Kabat	#	FR or CDR	Mouse 1D9 V <sub>H</sub>	Mouse IIIc		Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core		1D9 RH <sub>A</sub>	1D9 RH <sub>B</sub>	Comment
1	1	FR1	E	E*		E		s		E	E	
2	2		V	V		V		C		V	V	
3	3		Q	K*		Q		s		Q	Q	
4	4		L	L*		L*		C		L	L	
5	5		V	E		V		s		V	V	
6	6		E	E		E		c		E	E	
7	7		S	S		S*		c		S	S	
8	8		G	G		G*		c		G	G	
9	9		G	G		G*		c		G	G	
10	10		G	G*		G		c		G	G	
11	11		L	L		L		S		L	L	
12	12		V	V*		V		c		V	V	
13	13		Q	Q		Q	K	s		K	K	
14	14		P	P		P*		c		P	P	
15	15		K	G		G*	G	s		G	G	
16	16		G	G		G		s		G	G	
17	17		S	S		S*		c		S	S	
18	18		L	M*		L*		c		L	L	
19	19		K	K*		R	R	c		R	R	
20	20		L	L		L		c		L	L	
21	21		S	S		S*		c		S	S	
22	22		C	C		C*		C		C	C	
23	23		A	V		A		c		A	A	
24	24		A	A		A		C		A	A	
25	25		S	S		S*		c		S	S	
26	26		G	G		G		c		G	G	
27	27		F	F		F*		C		F	F	
28	28		S	T*		T	T	C		T	S	Δ1
29	29		F	F*		F		C		F	F	
30	30	FR1	N	S		S	S	S		S	N	Δ2
31	31	CDR1	A	N		S	N	c		A	A	
32	32		Y	Y		Y	A	S		Y	Y	
33	33		A	T		A	W	S		A	A	
34	34		M	M		M		c		M	M	
35	35		N	N		S	S	c		N	N	
35a			-	-		-		c		-	-	
35b		CDR1	-	-		-		c		-	-	

Figure 20A

Applicants: Ther sa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Kabat	#	FR or CDR	Mouse 1D9 V <sub>H</sub>	Mouse IIIc	Human III	Human Acceptor 4B4'CL (000490)	Surf- ace Or Core	1D9 RH <sub>A</sub>	1D9 RH <sub>B</sub>	Comment
36	36	FR2	W	W	W*		C	W	W	
37	37		V	V	V*		C	V	V	
38	38		R	R	R*		C	R	R	
39	39		Q	Q	Q*		c	Q	Q	
40	40		A	S	A		c	A	A	
41	41		P	P	P		s	P	P	
42	42		G	E	G*		s	G	G	
43	43		K	K	K		s	K	K	
44	44		G	G	G		c	G	G	
45	45		L	L	L*		C	L	L	
46	46		E	E*	E		C	E	E	
47	47		W	W	W*		C	W	W	
48	48		V	V*	V*		C	V	V	
49	49	FR2	A	A	S	G	C	G	G	
50	50	CDR2	R	E	V		c	R	R	
51	51		I	I	I		c	I	I	
52	52		R	R	S	K	s	R	R	
52a	53		T	L	G	S	s	T	T	
52b	54		K	K	K*		s	K	K	
52c	55		N	S	T	T	c	N	N	
53	56		N	H	D	D		N	N	
54	57		N	N	G	G		N	N	
55	58		Y	Y	G	G		Y	Y	
56	59		A	A	S	T	s	A	A	
57	60		T	T	T		c	T	T	
58	61		Y	H	Y	D	c	Y	Y	
59	62		Y	Y	Y		c	Y	Y	
60	63		A	A	A		c	A	A	
61	64		D	E	D	A	s	D	D	
62	65		S	S	S	P	s	S	S	
63	66		V	V	V*		c	V	V	
64	67		K	K	K		s	K	K	
65	68	CDR2	D	G	G*	G	s	D	D	
66	69	FR3	R	R	R*		C	R	R	
67	70		Y	F	F*	F	C	F	F	
68	71		T	T	T		C	T	T	
69	72		I	I*	I*		C	I	I	
70	73		S	S	S*		S	S	S	
71	74		R	R	R*		C	R	R	
72	75		D	D	D		c	D	D	
73	76		D	D	N		C	D	D	
74	77		S	S	S		s	S	S	
75	78		E	K	K	K	s	K	K	
76	79		S	S	N	N	s	N	N	
77	80		M	S	T	T	c	T	T	
78	81		L	V	L		C	L	L	
79	82		F	Y	Y	Y	c	Y	Y	
80	83		L	L	L*		c	L	L	

Figure 20B

Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Kabat	#	FR or CDR	Mouse 1D9 V <sub>H</sub>	Mouse IIIc	Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core	1D9 RH <sub>A</sub>	1D9 RH <sub>B</sub>	Comment
81	84		Q	Q*	Q		c	Q	Q	
82	85		M	M	M*		C	M	M	
82a	86		N	N	N		s	N	N	
82b	87		N	N	S	S	s	S	S	
82c	88		L	L	L*		c	L	L	
83	89		K	R	R		s	K	K	
84	90		T	A	A		c	T	T	
85	91		E	E	E		s	E	E	
86	92		D	D	D		C	D	D	
87	93		T	T	T		c	T	T	
88	94		A	G	A*		c	A	A	
89	95		M	I	V	V	c	V	V	
90	96		Y	Y	Y*		c	Y	Y	
91	97		Y	Y	Y*		C	Y	Y	
92	98		C	C*	C*		C	C	C	
93	99		V	T	A	T	C	T	T	
94	100	FR3	T	T	R		C	T	T	
95	101	CDR3	F	G	G	D	c	F	F	
96	102		Y	F	R	S	c	Y	Y	
97	103		G	-	x	L	s	G	G	
98	104		N	-	G	P	c	N	N	
99			-	-	x	P	c	-	-	
100			-	-	S	H	c	-	-	
100 a			-	-	L		C	-	-	
100 b			-	-	S		C	-	-	
100 c			-	-	G			-	-	
100 d			-	-	x			-	-	
100 e			-	-	Y			-	-	
100 f			-	-	Y			-	-	
100 g			-	-	Y			-	-	
100 h			-	-	Y			-	-	
100 I			-	-	H			-	-	
100 j			-	-	Y			-	-	
100 k			-	F	F		C	-	-	
101	105		G	A	D	R	C	G	G	
102	106	CDR3	V	Y	Y		C	V	V	
103	107	FR4	W	W	W*		C	W	W	
104	108		G	G	G*		C	G	G	
105	109		T	Q	Q	Q	S	Q	Q	
106	110		G	G	G*		C	G	G	
107	111		T	T	T*		C	T	T	
108	112		T	L	L	L	C	L	L	
109	113		V	V	V*		C	V	V	
110	114		T	T	T*		C	T	T	
111	115		V	V*	V*			V	V	
112	116		S	S	S*			S	S	
113	117	FR4	S	S	S*			S	S	

Figure 20C

Applicants: Theresa O'Keefe et al.

HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

ATGGACTTCGGGTAAACTTGGTTTCTTTTGTGTTTTTAACAAGGTGTCATTTGAGGTGCAGCTTGTGAGTCGGAGGAGGATTGGTGAGCCTA 100  
 TACCTGAAGCCCAATTGAACCAAGAAACAACAATAATAGTTCACACGTAACACTCCACGTGCAACAACCTCAGACCTCTCTCTAAACACGTCGGAT  
 M D F G L N L V F F V F Y Q G V H C E V Q L V E S G G L V Q P  
 leader ← variable  
 AAGGGTCATTGAAACICATGTGCAGCCTCTGGATTTCAGCTTCAATGCCCTACGCCATGAACTGGGTCCGCCAGGCTCCAGGAAGGGTTTGGAAATGGGT 200  
 TCCCAGTAACCTTGAGAGTACAGTCGGAGACCTAAGTCGAAGTTACGGATGCGGTACTTGACCCAGGCGGTCCGAGGTCTCTTCCCAACCTTACCCA  
 K G S L K L S C A A S G F S F N A Y A M N W V R Q A P G K G L E W V  
 TGCTGCATAAGAACTAAATAATAATTATGCAACATATTATGCCGATTTCAGTGAAGACAGATACACCAATCICCCAGAGATGATTCAGAAAGTATGCTC 300  
 ACGAGCGTATTTCTTGATTTTATTATTAATACGTTGTATAATACGGCTAAGTCACATTTCTGCTCTAGGTAGAGGTCTCTACTAAGTCTTTTCATACGAG  
 A R I R T K N N N Y A T Y Y A D S V K D R Y T I S R D D S E S M L  
 TTCTGCAATGAACAACCTTGAAACTGAGGACACAGCCCATGTATTACTGTGACCTTTTACGGTAACGGTGTCGGGACACAGGACCCACGGTCACCG 400  
 AAAGACGTTTACTTGTGAACCTTTGACTCCIGTGTCGGTACATAATGACACACTGGAAATGCCATTGCCACAGACCCCGTGTCCCTGGTGCCAGTGGC  
 F L Q M N N L K T E D T A M Y Y C V T F Y G N G V W G T G T T V T  
 TCTCTCAGCCAAACAACAGCCCCATCCGTCATCCCTGGT  
 AGAGGATCGGTTTTGTGTCGGGTAGGCAGATAGGGACCA 443  
 variable ← constant  
 V S S A K T T A P S V Y P L V

Figure 21

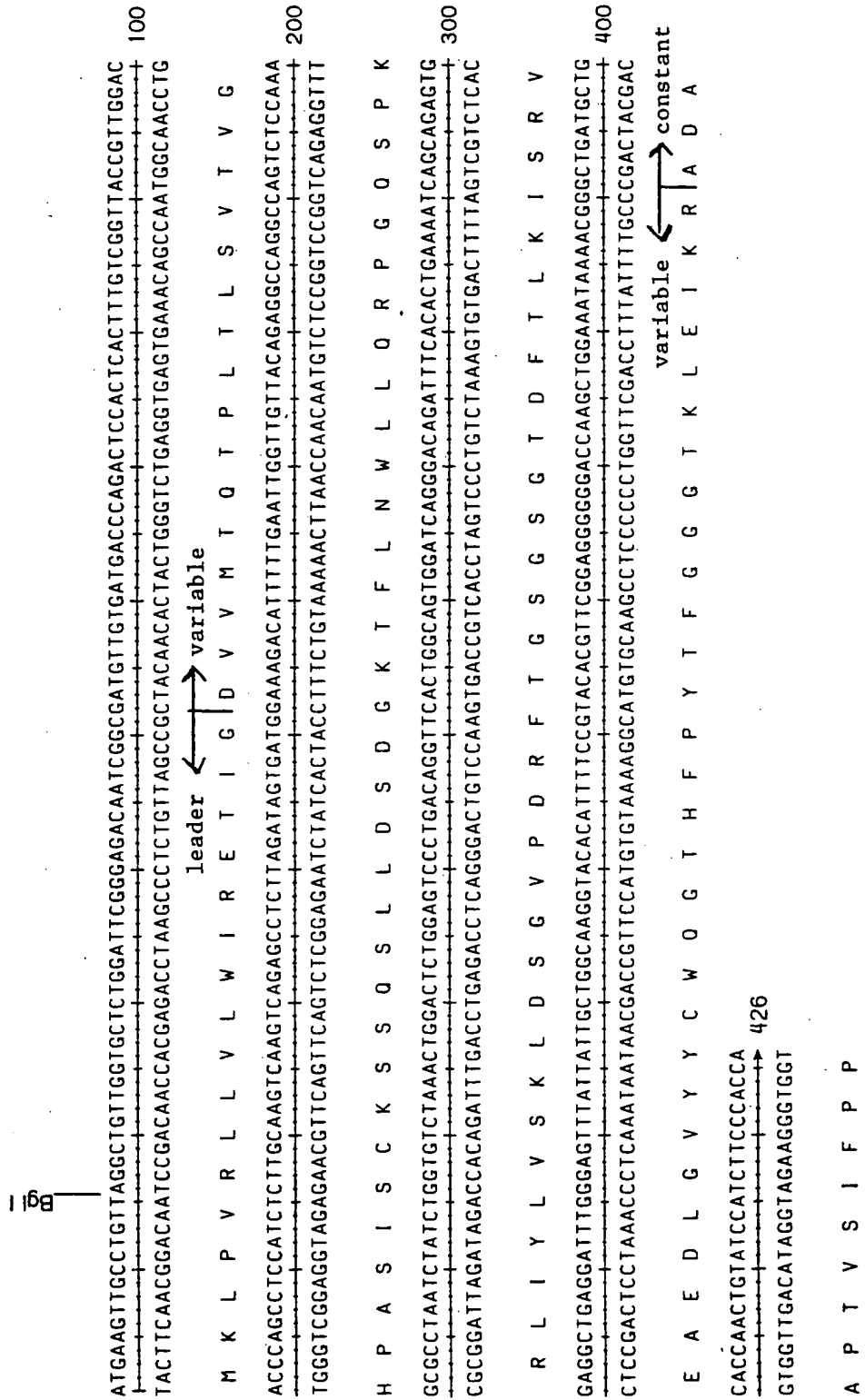


Figure 22

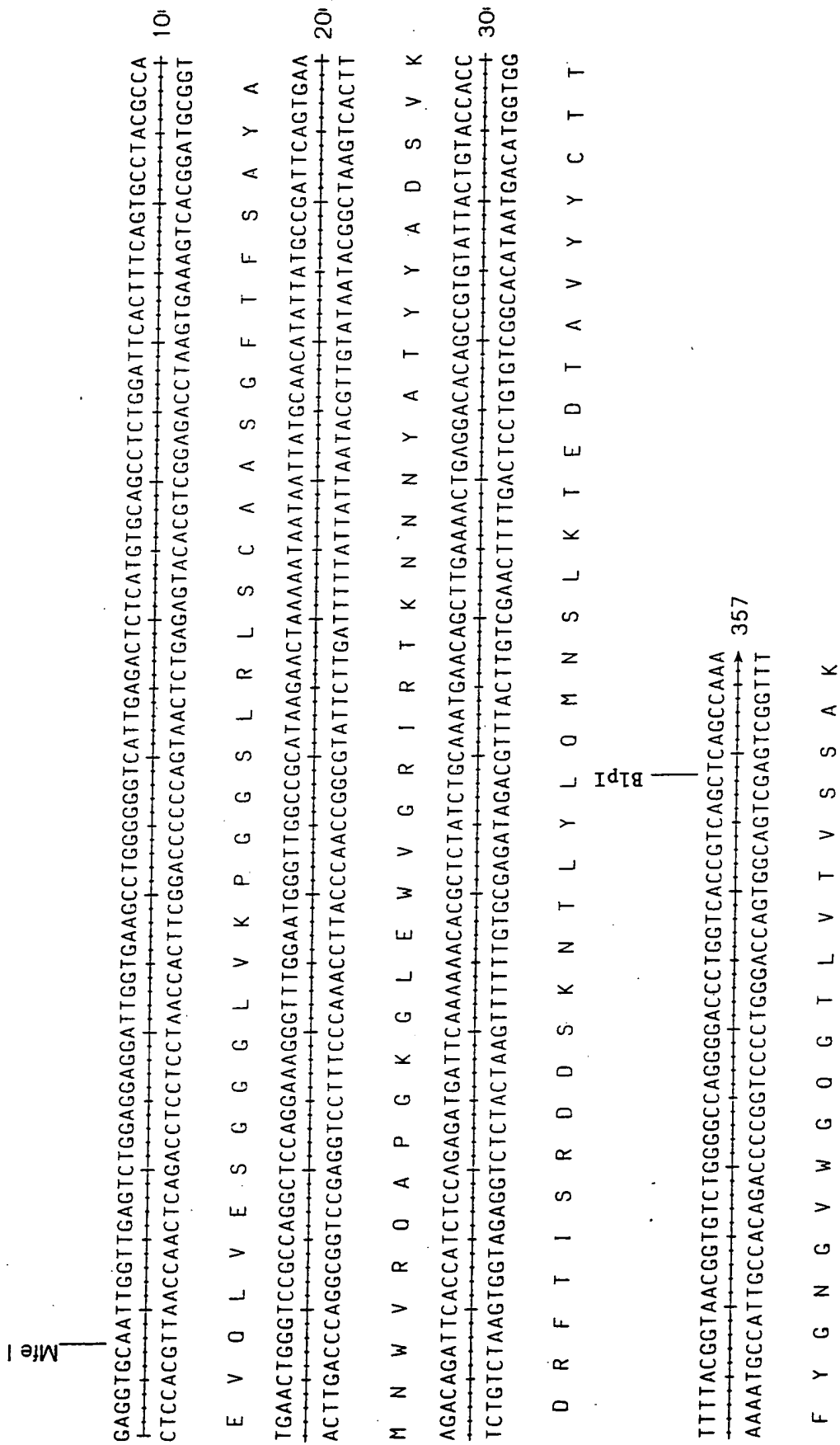


Figure 23

Applicants: Theresa O'Keefe et al.

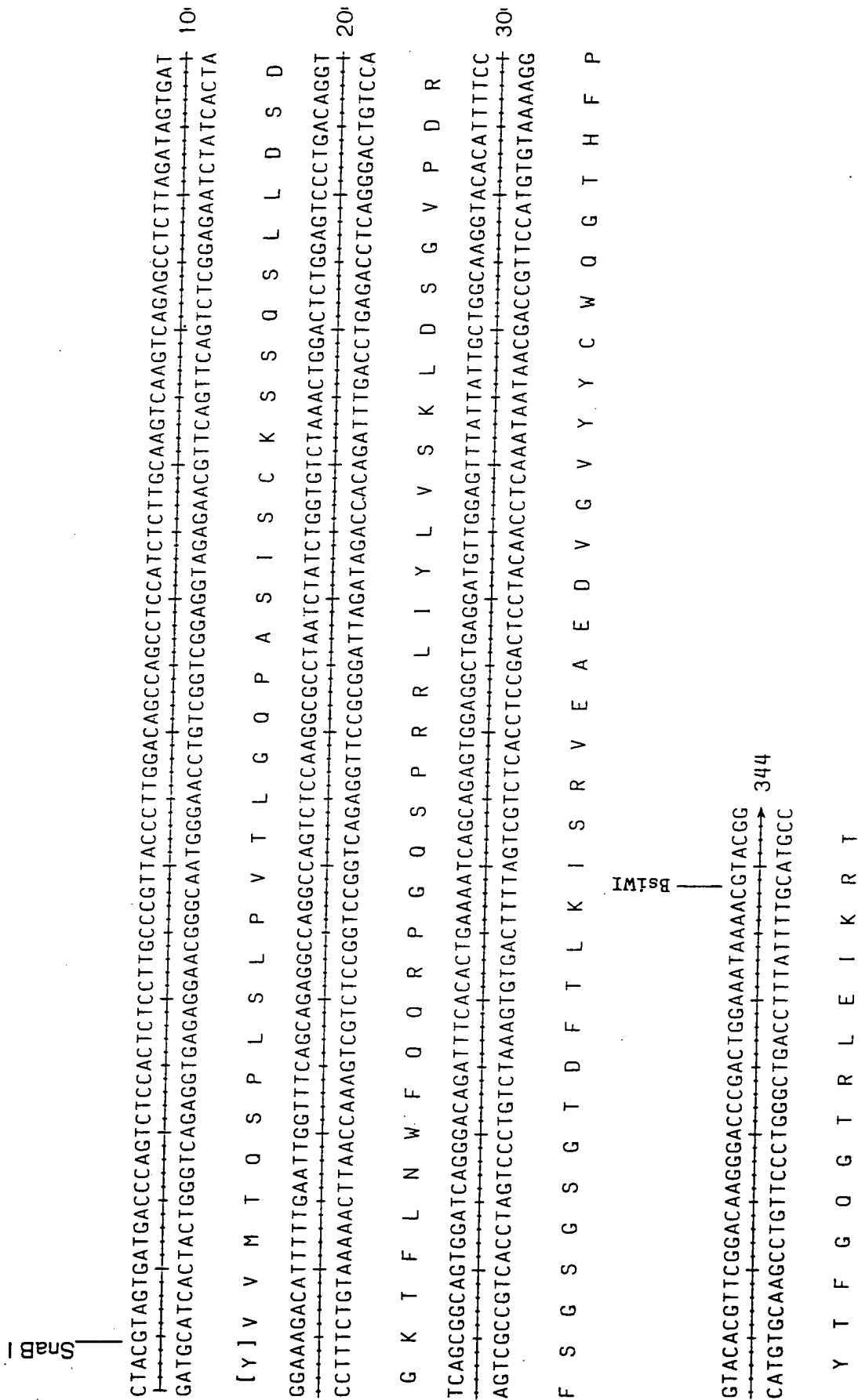
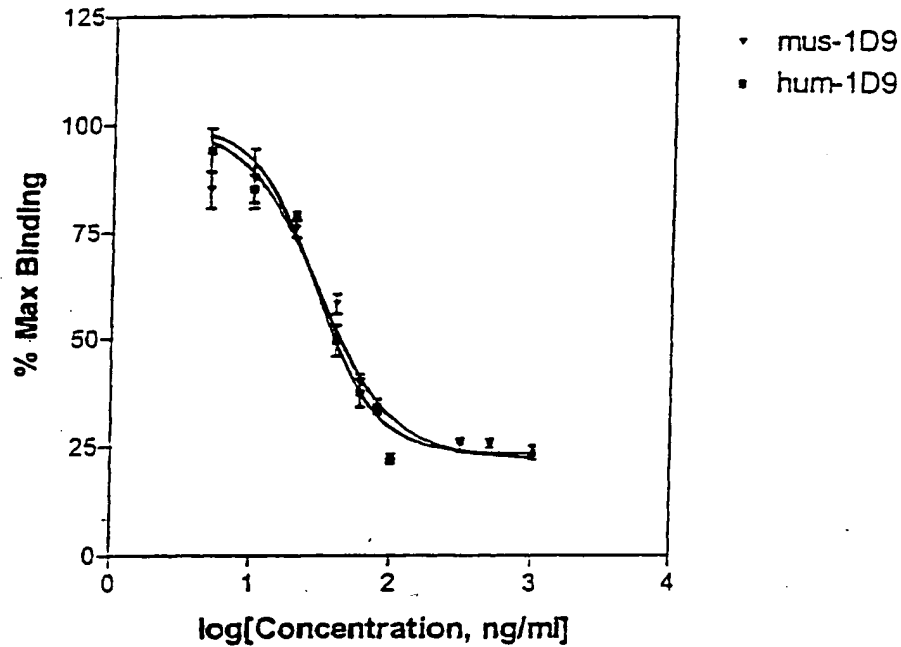
HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR

Figure 24

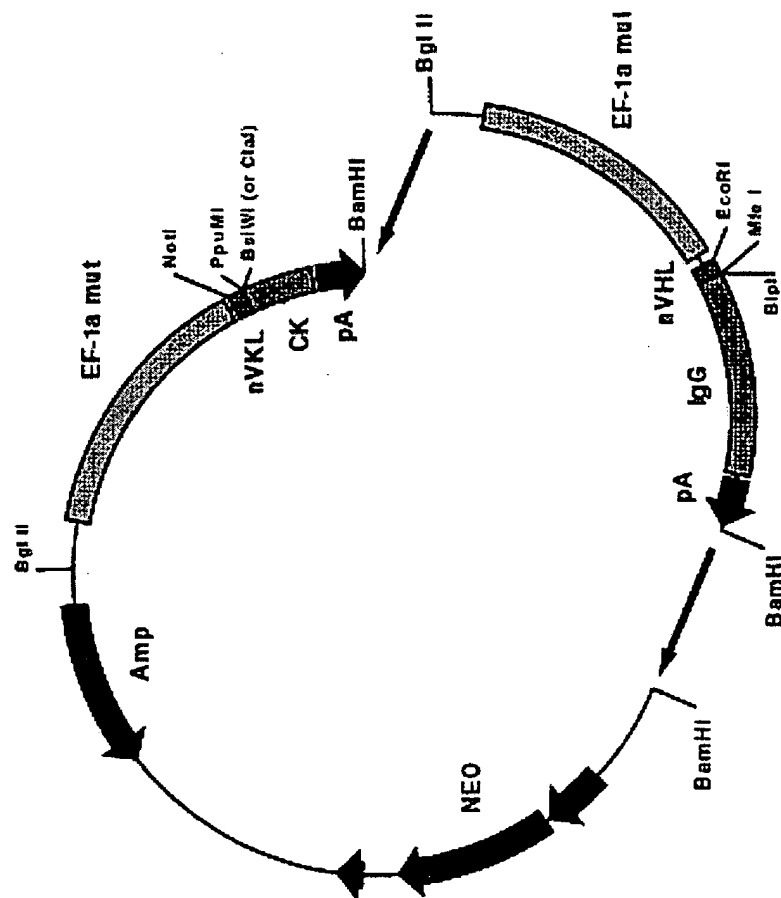
### Comparison of Humanized 1D9 vs. m1D9



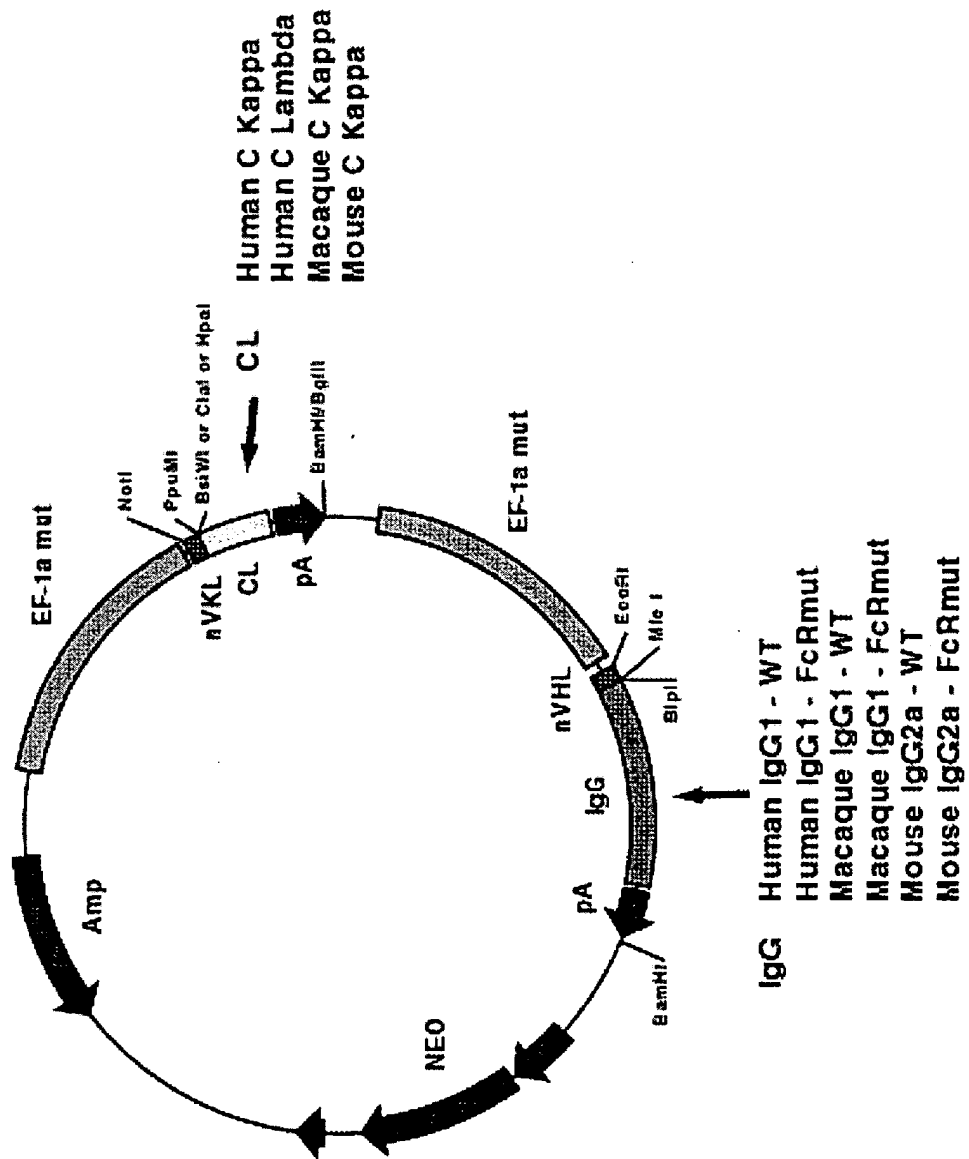
	hum-1D9	mus-1D9
Equation 1		
Best-fit values		
BOTTOM	23.46	22.40
TOP (Constant)	100.0	100.0
LOGEC50	1.452	1.472
HILLSLOPE	-1.972	-1.627
EC50	28.32	29.68
Std. Error		
BOTTOM	2.656	3.945
LOGEC50	0.04151	0.06251
HILLSLOPE	0.2946	0.3143
95% Confidence Intervals		
BOTTOM	17.18 to 29.74	13.07 to 31.73
LOGEC50	1.354 to 1.550	1.325 to 1.620
HILLSLOPE	-2.668 to -1.275	-2.370 to -0.8835
EC50	22.59 to 35.51	21.12 to 41.71
Goodness of Fit		
Degrees of Freedom	7	7
R squared	0.9931	0.9858
Absolute Sum of Squares	48.60	88.53
Sy.x	2.635	3.556
Data		
Number of X values	10	10
# of Y replicates (mean analyzed)	3	3
Total number of values	10	10
Number of missing values	20	20

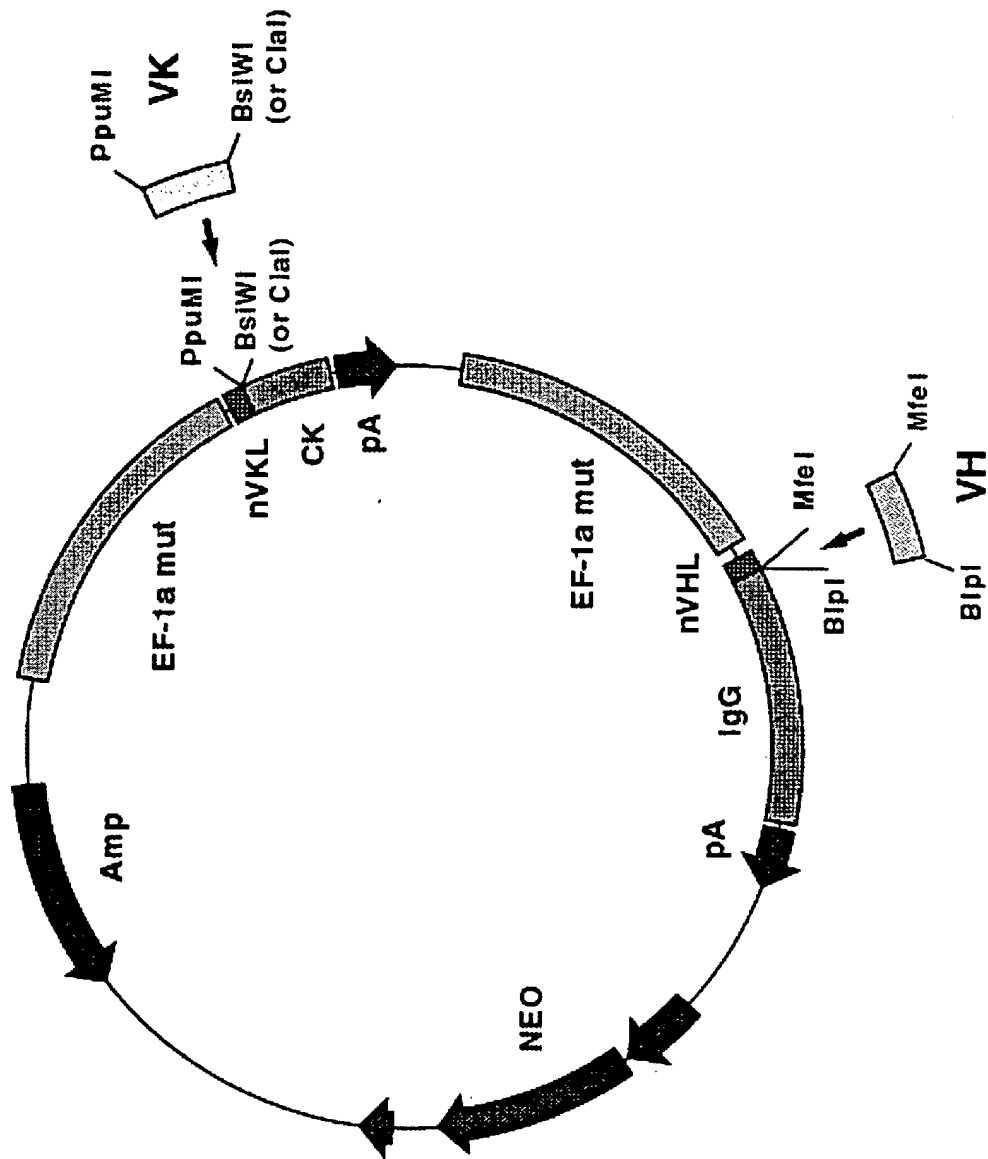
Figure 25



**Figure 26**

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HUMANIZED ANTI-CCR2 ANTIBODIES AND METHODS OF  
USE THEREFOR**Figure 27**

**Figure 28**